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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/344,676	06/25/1999	WILLIAM P. VAN ANTWERP	PD-0310	9328

22462 7590 09/23/2003  
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EXAMINER
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LUKTON, DAVID

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/23/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/344,676

Applicant(s)

VAN ANTWERP ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 26 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8, 9, 11, 14, 17, 19-21, 25-52, 58-62, 64-66 and 71 is/are pending in the application.
- 4a) Of the above claim(s) 8, 17, 26-52, 58 and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9, 21, 59, 61 and 65 is/are rejected.
- 7) ☒ Claim(s) 4-6, 11, 14, 19, 20, 25, 60, 62, 66 and 71 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

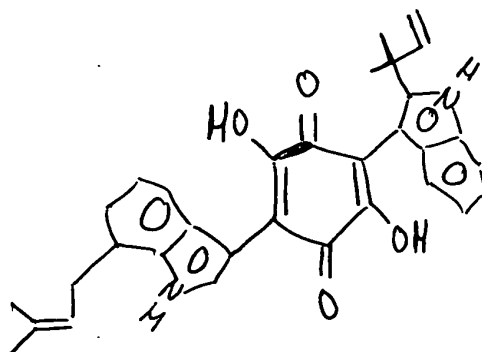
Pursuant to the directives of paper No. 20 (filed 6/26/03), claims 1, 11, 14, 17, 19-21, 34, 41, 51, 58-60, 66, 71 have been amended, and claims 7, 12, 13, 22, 23, 54, 63, 67, 68 cancelled. Claims 1-6, 8, 9, 11, 14, 17, 19-21, 25-52, 58-62, 64-66, 71 are now pending. Claims 8, 17, 26-52, 58, 64 remain withdrawn from consideration.

Claims 1-6, 9, 11, 14, 19-21, 25, 59-62, 65, 66, 71 are examined in this Office action. Applicants' arguments filed 6/26/03 have been considered and found persuasive. The previously imposed §103 rejections are withdrawn. However, in view of the claim amendments, new grounds of rejections are now imposed. The claims that are objected to are so characterized because of their dependence on rejected claims.

\*

Claim 61 is rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In claim 61, the term "L-783281" may be used if accompanied by the chemical name that this term represents. If the chemical name is not available, the structure may be provided instead, i.e., the following:



\*

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-3, 9, 21, 59 and 65 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* 13 (2) 75-7, 1990) in view of Rieveley (USP 6,153,632).

Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer.

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition

comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Rieveley does not explicitly state that “insulin” is a peptide which is “related” to insulin, and Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol.

With respect to claim 1, an “insulin-related peptide” or an “insulin-related peptide analog” could be viewed as encompassing insulin itself. According to one interpretation, insulin could even be regarded as the epitome of an “insulin-related peptide” or an “insulin-related peptide analog”. Thus, insulin itself is fulfilling the roles of agents (i) and (ii). A similar argument applies in the case of claim 59.

Thus, the endocrinologist of ordinary skill would have been motivated to use the surface-active stabilizer polyethylene - polypropylene glycol in order to reduce catheter occlusion and to achieve a “significant improvement of metabolic control”. The endocrinologist of ordinary skill would have been motivated to use the insulin sensitizer to enhance insulin uptake and/or utilization of glucose by the cells of the patient. Thus, by combining the teachings of Walter and of Rieveley, the artisan of ordinary skill would arrive at the claimed composition. The claims are thus rendered obvious.

✱

Claims 1-3, 9, 21, 59 and 65 are rejected under 35 U.S.C. §103 as being unpatentable over Grau (*Diabetes* 36 (12) 1453-1459, 1987) in view of Rieveley (USP 6,153,632).

Grau discloses (page 1453, col 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed is that the "HOE 21 PH" reduces the precipitation and catheter occlusion that would otherwise occur with insulin alone. Grau conveys that "HOE 21 PH" insulin is advantageous when used with insulin infusion pumps. Grau does not suggest combining insulin with an insulin sensitizer.

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Rieveley does not explicitly state that "insulin" is a peptide which is "related" to insulin, and Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol.

With respect to claim 1, an "insulin-related peptide" or an "insulin-related peptide analog" could be viewed as encompassing insulin itself. According to one interpretation, insulin could even be regarded as the epitome of an "insulin-related peptide" or an "insulin-related peptide analog". Thus, insulin itself is fulfilling the roles of agents (i) and (ii). A similar argument applies in the case of claim 59.

Thus, the endocrinologist of ordinary skill would have been motivated to use the surface-active stabilizer polyethylene - polypropylene glycol in order to reduce precipitation and catheter occlusion. The endocrinologist of ordinary skill would have been motivated to use the insulin sensitizer to enhance insulin uptake and/or utilization of glucose by the cells of the patient. Thus, by combining the teachings of Grau and of Rieveley, the artisan of ordinary skill would arrive at the claimed composition. The claims are thus rendered obvious.

\*

Claims 1-3, 9, 21, 59 and 65 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* **13** (2) 75-7, 1990) in view of Clark (USP 5,783,556) further in view of Rieveley (USP 6,153,632).

As indicated above, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer or with IGF-I.

As indicated previously, Clark discloses a composition comprising insulin and IGF-1. It is disclosed (e.g., col 20, line 52+ ) that coadministration of insulin and IGF-I leads to unexpectedly lower glucose levels, which is advantageous in the management of diabetic patients. Clark does not disclose the use of insulin sensitizers.

As indicated previously, Rieveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Riveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol or with IGF-I.

The practitioner of the Walter invention would be in possession of a combination of insulin and polyethylene - polypropylene glycol which could be used for treatment of diabetes. The artisan of ordinary skill would take from Clark the disclosure that coadministration of insulin and IGF-I leads to unexpectedly lower glucose levels, which is advantageous in the management of diabetic patients. The artisan of ordinary skill would take from Rieveley the disclosure that by combining insulin with an insulin sensitizer, the result is that the cells of the patient will be sensitized so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required.

Accordingly, the artisan of ordinary skill would have been motivated to combine insulin with polyethylene - polypropylene glycol, amylin and an insulin sensitizer. Thus, the claims are rendered obvious.

✱

Claims 1-3, 9, 21, 59 and 65 are rejected under 35 U.S.C. §103 as being unpatentable over Walter H. M. (*Diabetes Research* 13 (2) 75-7, 1990) in view of Cooper (USP 5,641,744),

further in view of Rieveley (USP 6,153,632).

As indicated above, Walter discloses (page 76, col 1, paragraph 2) "HOE 21 PH" insulin which is insulin combined with the surface-active stabilizer polyethylene - polypropylene glycol. Also disclosed (e.g., page 76 col 2) that use of the "HOE 21 PH" insulin resulted in less catheter occlusion and a "significant improvement of metabolic control". Walter does not suggest combining insulin with an insulin sensitizer or with amylin.

As indicated previously, Cooper discloses (e.g., col 3, line 37+) a composition comprising insulin and amylin. Cooper also discloses (col 3, line 57+) that the combination provides "tighter diabetic control with reduced risk of hypoglycemia". Cooper does not disclose the use of insulin sensitizers.

As indicated previously, Riveley discloses (e.g., col 4, line 50+) a composition comprising insulin and an insulin sensitizer. As stated (col 4, line 56+), the effect of the insulin sensitizer is to sensitize the cells of the mammal so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required. Rieveley does not teach combining insulin with the surface-active stabilizer polyethylene - polypropylene glycol, or with amylin.

The practitioner of the Walter invention would be in possession of a combination of insulin and polyethylene - polypropylene glycol which could be used for treatment of diabetes.

The artisan of ordinary skill would take from Cooper the disclosure that combining insulin with amylin will produce "tighter diabetic control with reduced risk of hypoglycemia".

The artisan of ordinary skill would take from Rieveley the disclosure that by combining insulin with an insulin sensitizer, the result is that the cells of the patient will be sensitized so as to enhance insulin uptake and/or utilization of glucose by the cells of the mammal thus reducing the therapeutic dose of insulin that is required.

Accordingly, the artisan of ordinary skill would have been motivated to combine insulin with polyethylene - polypropylene glycol, amylin and an insulin sensitizer. Thus, the claims are rendered obvious.



No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*D. Lukton* 9/17/03

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